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SUMMARY

Manned Apollo missions have provided the opportunity to study fluid/electrolyte and endocrine homeostasis in space crewmen. These studies have been conducted by our laboratory principally for two reasons. First, experience gained from Mercury, Gemini, and early Apollo missions showed dynamic postflight changes in water retention, electrolyte balance, and changes in hormones active in fluid and electrolyte control. Commensurate with these changes were the physical and clinical characteristics of the crewmen returning from space flight.

The comparable protocol has been implemented in most of the Apollo missions. Deviations from this procedure have been because of the constraints imposed by quarantine missions. Blood and 24-hour urine specimens were obtained 1, 2, and 4 weeks before the missions to establish the crew health status and baseline values for postflight comparisons. Postflight samples were obtained as soon as possible, 1, 2, 6, and 13 days immediately after recovery. The results reflected changes incurred during space flight as well as those caused by the return to earth gravity. The data that are suggestive of inflight changes include

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decreases in exchangeable potassium (15 percent) and serum potassium (5 percent) combined with decreased urine sodium (49 percent) and potassium (37 percent) without a significant change in urinary sodium/potassium ratio. A mean increase in titratable acid (228 percent) was measured. These variables suggest that aldosterone secretion was increased during space flight and that the resultant increase in this steroid was related in part to the measured potassium loss. The physiological attempt to increase circulating blood volume in response to return to the 1-g environment was demonstrated by increased angiotensin I (700 percent), aldosterone (98 percent), and antidiuretic hormone (400 percent) with a decrease in urine volume (20 percent) in the first 48 hours after return to earth. These changes are not considered to be because of decrements in overall renal function because blood urea nitrogen and creatinine were unchanged.

Consistent with these measurements was a mean 5.6 percent decrease in plasma volume on those missions during which this measurement was made. Although these changes are less than would be predicted from bedrest studies, the decrement measured over five missions is different statistically from zero ($P < 0.005$). The extracellular fluid determinations have shown a slight decrease postflight; however, this decrement is within the experimental error of the method. On those six crewmen tested, all have shown a significant postflight decrease in total body water.

Although the limited amount of data collected throughout manned space flight has demonstrated essentially consistent trends, the Apollo 15 experiences indicate a disparity from previous presentations. The Apollo 15 crewmen showed an atypical polyuria in the presence of elevated urinary antidiuretic hormone levels postflight. This is suggestive of a distal tubular imbalance in sodium, potassium, and water transport. Whether this imbalance is related to the measured potassium deficit, to other predisposing mechanisms, or to both is not known. The increase in titratable acidity is consistent with an acidemia; however, the etiology of such an event may not be related to the decrease in total body potassium concentration.

The measured changes are consistent with the prediction that a relative increase in thoracic blood volume upon transition to the zero-g environment is interpreted as a true volume expansion resulting in an osmotic diuresis. This diuresis, in association with other factors, ultimately results in a reduction in intravascular volume leading to increased renin activity and a secondary hyperaldosteronism. Once these compensatory mechanisms are effective in reestablishing a state of euhydration, the crewmen are considered to be adapted essentially to the zero-g environment. Although the physiological cost of this adaptation must reflect the potassium deficit and, perhaps, other factors, it is assumed that the compensated state is adequate for the demands of the environment. The effects of superimposed clinical insults, particularly emunctory and insensible salt and water loss, fatigue, and emotional factors, cannot be minimized. During the remaining Apollo flights and the Skylab Program, attempts will be made to resolve this problem. Inflight urine collections in Apollo 16 and 17 and inflight urine and blood sampling in the Skylab Program predictably will offer information that will better define the mechanisms operative in fluid and electrolyte homeostasis in space flight.

INTRODUCTION

With the December launch of Apollo 17, the NASA brings to an end the highly successful Apollo Program. The complexities of multiple docking in space, landing on the moon, and returning to orbit required emphasis on engineering and navigation, whereas biological studies took a subsidiary role. As the missions became more routine, the medical directorate under Dr. Charles A. Berry was given authority to perform progressively more complex physiological studies designed to ensure the medical safety of the crewmen and to describe the adaptive processes in the weightless environment. The task of the overall operational medical program was to study the endocrine and fluid volume changes of the returning crewmembers.

Before Apollo 7, considerable knowledge had been accumulated concerning the fluid and endocrine changes associated with the Mercury and Gemini earth orbital missions. For example, it was known that astronauts always weighed less on their return to earth than they did before the mission. Generally, this decrease in weight was interpreted as cardiovascular deconditioning and was associated with modest decreases in plasma volume. These results showed that although cardiovascular deconditioning was similar to that deconditioning found after bedrest studies, the fluid changes after weightlessness were greater but the plasma volume changes smaller. After Gemini, there was evidence that the entry sequence caused a sudden increase in epinephrine release. This release was indicated by a short-lived granulocytosis. Also, these findings indicated that entry and recovery were stressful experiences. Before Mercury, there was considerable apprehension among the medical monitors that weightlessness would produce life-threatening hypercalcemia and hypercalciuria. This apprehension subsided when no evidence of a calcium abnormality was found. Even after the 14-day Gemini VII mission, X-ray bone densitometry showed moderate or nonexistent loss of bone mineral. From this background, the more extensive endocrine and metabolic studies were planned for Apollo VII and have been continued to the most recent mission (Apollo 16). As with other portions of the medical program, these studies were designed to assist the medical monitors in maintaining the health of crewmembers during the mission. Some of the findings from these studies have been reported to this society in past years by Dr. Charles A. Berry. It is our purpose to summarize the endocrine and metabolic results obtained before and after the Apollo missions. From these results, it is possible to obtain an idea of the nature and extent of the crewmember endocrine adaptation.

METHODS

The same general protocol has been followed for most of the Apollo missions. Deviations from these procedures have been only because of the constraints imposed by the quarantine missions (Apollo 11, 12, and 14).

With crewmembers reclining for 30 minutes, approximately 45 milliliters of peripheral venous blood was drawn 15 days before space flight and approximately 2 hours after recovery. All of the blood samples were drawn with the subject fasting at 7:30 to 8:00 a.m., except the sample drawn as soon as possible (ASAP) after splashdown. At 15-days preflight (F-15), the crewmembers had been ambulatory less than 1 hour.

Twenty-four hour urine samples were collected from each crewman on the same day as the blood workup. The pooled urine was collected (with no additive), aliquoted, stabilized (with acid), and frozen for future analysis.

Ground-based control subjects have been used during each mission as a quality check on the effects of collection and transport of biological samples. The results showed that transporting the samples to the NASA Manned Spacecraft Center (MSC) produced no change in the values.

Analyses on the blood (plasma or serum) samples included, among others, osmolality, sodium, potassium, chloride, adrenocorticotrophic hormone (ACTH), angiotensin I, hydrocortisone, creatinine, blood urea nitrogen (BUN), calcium, phosphorus, magnesium, and parathormone (PTH). The 24-hour urine samples were analyzed for electrolytes, osmolality, volume, creatinine, aldosterone, and antidiuretic hormone (ADH).

All data were analyzed by a two-way analysis of variance and the standard error of the mean was calculated from the error mean square. In all cases, data obtained 15 days immediately preceding the flight were used for the control data point and the data obtained immediately postflight were compared with this preflight control.

RESULTS

Postmission body fluid losses have been found in crewmen of both American and Russian manned space flights. Nearly every crewman has shown a 2.5 to 5.0 percent decrease in body weight postflight. In Apollo, this loss averaged 6 pounds or a mean weight loss of 3.8 percent ± 2.3 SD. Over 50 percent of the weight was regained within the first 24 hours after recovery.

These body weight changes have indicated significant fluid changes among all crewmembers exposed to weightlessness (table I). This fluid and tissue loss does not seem to be related to the duration of the mission. Because of this, studies were undertaken to investigate the cations and anions that serve critical roles in the homeostatic regulation of fluid volume. Serum-electrolyte data from the Apollo crewmen are summarized in table II. It was observed that there is a 7 percent decrease in serum potassium, a 0.9 percent decrease in the serum sodium, and a 5 percent decrease in magnesium immediately postflight. These changes were accompanied by no change of statistical significance in chloride or osmolality.

The 24-hour urine samples obtained at the time of these serum samples exhibited significant changes when the immediate postflight samples are compared with the control samples acquired 15 days before flight. The electrolyte analysis is shown in table III. In the first 24 hours after flight, sodium, potassium, magnesium, and chloride are decreased significantly.

To aid in the understanding of water, electrolyte balance, and renal function, renin activity was measured as angiotensin I in blood samples and the adrenal mineral corticoid and aldosterone was measured in the urine (table IV). The plasma angiotensin I values show a 555 percent increase in the crewmen tested on the day of recovery. This elevation is followed by a significant increase (62 percent) in urinary aldosterone during the first day following recovery.

The summary data on urinary volume, antidiuretic hormone, and osmolality are shown in table V. These results indicate a 39 percent decrease in urine volume postflight with significant increases in osmolality (24 percent) and ADH (339 percent).

Plasma cortisol and ACTH results are given in table VI. Although no significant change was found, a mean decrease was demonstrated.

Table VII contains the BUN and creatinine clearance data. The creatinine clearance results indicate no significant change in renal function postflight. A slight increase in BUN was found.

The calcium and phosphorus changes are summarized in table VIII along with the PTH from the two missions from which these results were obtained. It is thought that the calcium, phosphate, and PTH results not only reflect normal bone metabolism but also give evidence of normal renal function. These results are in agreement with photon absorptiometry studies conducted on several Apollo flights that showed small to insignificant losses of bone calcium following these missions.

There has been a mean 5.6 percent decrease in plasma volume after those missions in which this measurement was made. Although these changes are less than would be predicted from bedrest studies, the decrement measured over five missions is different statistically from zero ($P < 0.005$).

DISCUSSION

Taking into consideration all of these data along with the clinical condition of the returning Apollo crewmen, the following hypothesis has been proposed to explain these changes. As a crewman enters the weightless environment, his circulating blood volume and extracellular fluid is redistributed from the dependent extremities and the lower abdomen equally throughout the vascular space. This equalization of the blood volume is interpreted as a relative volume expansion. This fluid redistribution necessitates a compensatory change in water balance with a net loss of fluid and electrolytes. The extent of the fluid and electrolyte loss is related also to dietary intake that has been both variable and generally below basal requirements during the first 24 hours of the mission. It is thought that principal changes in water balance occur within the first or second day as they do during bedrest studies. This would explain why the crewmembers show weight decreases even after short Mercury and Gemini missions.

During the return to a 1-g environment, 50 percent of the weight loss is regained within the first 24 hours. A rapid weight gain of this magnitude supports a profound renal and endocrine response to this new environment.

It is believed that the rest of the weight loss can be accounted for by loss of cellular mass. Consistently measured decreases in red cell mass and decreases in individual cell electrolyte content support this hypothesis. Furthermore, significant decrease in serum magnesium indicate losses in intracellular electrolyte concentrations because magnesium along with potassium is concentrated in the intracellular space.

A 20 percent postflight decrease in total body potassium has been measured by gamma spectrometric measurement of the total body potassium 40. In the Apollo 15 mission, total body exchangeable potassium was measured. It was found to be decreased about 13 percent even though adequate dietary potassium had been ingested throughout the mission. The crewmembers of the Gemini VII mission demonstrated positive potassium balance before and after the flight with a negative balance during the mission. The Gemini VII results were accompanied by increased urinary aldosterone excretion during the flight. These Gemini results and the data available from crewmen of the Apollo missions suggest that aldosterone is elevated during space flight. This elevation could be produced by decreases in renal blood flow, and decreases in carotid artery or right heart pressures. The specific etiology of this event must await further experimentation.

During the recovery operations the crewmen are exposed to increased ambient temperature in the spacecraft, helicopter, and on the carrier deck (because of the tropical location of the recovery operations). The crewmen do not eat or drink between the time they leave the spacecraft and the blood drawing. Thereafter, they can eat or drink anything they desire. The postrecovery diet is generally a high-salt, high-protein, and high-calorie diet. Generally, the postrecovery urine shows increased osmolality with a decrease in electrolyte content. This combination indicates increased excretion of nonelectrolyte osmotic substances. Part of this increase in osmolality may be a result of the increased BUN found postrecovery. The clinical laboratories have found similar elevations in uric acid. Because of the increased environmental heat during the first 4 hours after recovery, a slight increase in serum sodium and later in osmolality was expected. Serum sodium was actually less postmission than before the mission. Osmolality is unchanged. This suggests that serum sodium may have been even lower before reentry. This combined with the BUN change suggests that renal blood flow is decreased during weightlessness and this could be, in part, responsible for the increased aldosterone excretion by means of the renin-angiotensin system.

Balakhovshiy has suggested that the postflight weight loss in the American astronauts was because of dehydration caused by environmental temperatures in the tropical recovery zones. Our data do not substantiate dehydration as the causative factor for the fluid and electrolyte results because serum osmolality was not changed significantly postflight.

At recovery, there is an increase in catecholamine excretion associated with an increase in the number of circulating granulocytes. It would be logical to expect a similar increase in ACTH and cortisol excretion at that time. Present data show no evidence of cortisol and ACTH increase. Thus, we can assume that the stress of reentry is not great enough to produce a change in these hormones; however, the time of recovery is generally at a different point in the diurnal cycle of the pituitary-adrenal axis than is the preflight control. Without stress, higher values are expected at the time of the control specimens (8:00 a.m.) than at the time of recovery (anywhere from morning to early afternoon). Thus, the reentry stress may have elevated these hormones compared with what they would have been 24 hours before recovery.

Prolonged bedrest is associated with a negative calcium balance, particularly in the second week. It has been postulated that exposure to weightlessness would produce similar losses of calcium from the skeleton. The results of the Apollo missions do not seem to substantiate this. No increase in parathormone has been found at recovery; urine and serum calcium have not been elevated and bone densitometry has failed to show consistent decreases in bone mass. Therefore, we can conclude that for missions for as long as 14 days, significant calcium loss does not occur and hypercalcemia does not account for the loss of sodium.

TABLE I.- WEIGHT CHANGE SUMMARY IN APOLLO ASTRONAUTS

[Apollo 13 data not included]

	Number of subjects	Mean weight loss, lb	Mean change, percent	Mean weight regained, lb (R+24 hr)	Mean change, percent
All crewmembers on Apollo missions 7, 8, 9, 10, 11, 12, 14, and 15	24	-5.8	-3.5	+3.0	+1.9
Nonlunar EVA crewmen	16	-6.8	-4.1	+3.1	+1.9
Lunar EVA crewmen	8	-3.8	-4.0	+2.9	+1.8

TABLE II.- SERUM ELECTROLYTES

Electrolyte	Number	F-15 mean ± SE	ASAP mean ± SE	Percent change (a)	Significance
Sodium, Na, mEq/liter	27	142 ± 0.2	140 ± 0.4	0.9 (-)	P < 0.025
Potassium, K, mEq/liter	26	4.1 ± 0.06	3.8 ± 0.06	7.0 (-)	P < 0.005
Chloride, Cl, mEq/liter	25	104 ± 0.6	103 ± 0.6	1.2 (-)	P < 0.10
Magnesium, Mg, mg/100 ml	26	2.2 ± 0.05	2.1 ± 0.05	5.0 (-)	P < 0.001

[a](-) = decrease.

TABLE III.- URINE ELECTROLYTES

Electrolyte	Number	F-15 mean ± SE	ASAP mean ± SE	Percent change (a)	Significance
Na, mEq/vol	20	175 ± 15	97 ± 11	44 (-)	P < 0.01
K, mEq/vol	20	74 ± 6	46 ± 4	38 (-)	P < 0.001
Cl, mEq/vol	20	165 ± 15	74 ± 9	55 (-)	P < 0.001
Mg, mg/vol	17	9.5 ± 0.5	6.8 ± 0.7	28 (-)	P < 0.005

[a](-) = decrease.

TABLE IV.- ELECTROLYTE CONTROL PARAMETERS

Test	Number	F-15 mean + SE	ASAP mean + SE	Percent change (a)	Significance
Plasma angiotensin, mμg/ml/hr	14	2.0 ± 0.5	13.1 ± 3.0	555 (+)	P < 0.005
Urine aldosterone μg/volume	17	14.3 ± 2	23.2 ± 2	62 (+)	P < 0.005

[a](+) = increase.

TABLE V.- URINE CONCENTRATING PARAMETERS

Test	Number	F-15 mean ± SE	ASAP mean ± SE	Percent change (a)	Significance
Urine volume, ml	20	1711 ± 179	1048 ± 99	39 (-)	P < 0.005
Osmolality, mOsmo	20	735 ± 47	908 ± 41	24 (+)	P < 0.005
ADH, mU/volume	16	17.3 ± 3	75.9 ± 22	339 (+)	P < 0.025

[a](-) = decrease, (+) = increase.

TABLE VI.- ADRENAL-PITUITARY MEASUREMENTS

Test	Number	F-15 mean ± SE	ASAP mean ± SE	Percent change (a)	Significance
Hydrocortisone, μg/100 ml	23	14.8 ± 0.8	12.3 ± 2.0	17 (-)	P < 0.25
ACTH, pg/ml	6	46 ± 10	30 ± 5	35 (-)	P < 0.25

[a](-) = decrease.

TABLE VII.- RENAL FUNCTION MEASUREMENTS

Test	Number	F-15 mean ± SE	ASAP mean ± SE	Percent change (a)	Significance
BUN, mg/100 ml	29	18.2 ± 0.5	20.8 ± 0.7	14 (+)	P < 0.001
Creatinine clearance, 1/24 hr	26	148 ± 9	138 ± 9	7 (-)	P > 0.25

[a](-) = decrease, (+) = increase.

TABLE VIII.- CALCIUM METABOLIC MEASUREMENTS

Test	Number	F-15 mean ± SE	ASAP mean ± SE	Percent change (a)	Significance
Calcium serum, mg/100 ml	26	9.6 ± 0.06	9.7 ± 0.06	1 (+)	P > 0.25
Urine, mg/vol	17	103 ± 9	93 ± 11	10 (-)	P > 0.25
Phosphorus serum, mg/100 ml	26	3.5 ± 0.07	3.6 ± 0.10	3 (+)	P > 0.25
Urine, mg/vol	17	1038 ± 77	1067 ± 85	3 (+)	P > 0.25
Parathormone serum, pg/ml	6	0.34 ± 0.03	0.28 ± 0.06	18 (-)	P > 0.25

[a](-) = decrease, (+) = increase.